

*Appl. No. 09/851,058*

*Amendment dated July 1, 2004*

*Reply to Office Action of March 10, 2004*

### **REMARKS**

Applicants wish to thank Examiner Cook and Primary Examiner Nguyen for their time, helpful suggestions and recommendations during the personal interview on June 10, 2004, in which the outstanding rejections were discussed in relation to the pending claims. As a result, Applicants submit this Response.

#### **Interview Summary**

Primary Examiner Thuy Nguyen, Examiner Lisa Cook, and Applicants' representatives, Andrew T. Karnakis, Esq. and Michael J. Bastian, Esq., participated in the personal interview of June 10, 2004. Examiner Cook and Primary Examiner Nguyen and Applicants' representatives discussed the patentability of pending claims 1-22, in view of the outstanding rejections under 35 U.S.C. §103, as well as possible amendments to overcome the rejections under 35 U.S.C. §112. While agreement was not reached with respect to patentability, discussion around the §112 issues and Applicants desire to incorporate previously submitted claim language to describe the nature of the labeled protein reagents was deemed acceptable.

#### **Status of the Claims**

Claims 1-22 are pending in the application. Applicants hereby amend claims 1, 13, 16, 18 and 21. After entry of this paper, claims 1-22 remain pending for examination.

#### **Amendments to the Specification**

Applicants have amended the Abstract to avoid the objection in the Office Action with respect to the introduction of new matter and to bring the Abstract into conformity with the amended claims. Support for this amendment is found at least at page 10, lines 18-22. This amendment adds no new matter.

*Appl. No. 09/851,058*

*Amendment dated July 1, 2004*

*Reply to Office Action of March 10, 2004*

**Amendments to the Claims**

Applicants have amended claim 1. Support for the amendments to claim 1 is found at least at page 8, lines 1-19 and page 21, line 14 to page 24, line 15. Accordingly, the amendment to claim 1 adds to new matter.

Applicants have amended claims 3, 16, 18 and 21 to further clarify their dependency from claim 1. Support for these amendments is found at least at the same portions of the specification referenced with respect to the amendment to Claim 1. Accordingly, the amendments to claims 13, 16, 18 and 21 add no new matter.

**Rejections Under 35 U.S.C. §112**

Claims 1-22 were rejected under 35 U.S.C. §112, first paragraph, as allegedly failing to comply with the written description requirement as the Office Action asserts that the claims contain subject matter not described in the specification in a way to reasonably convey to one skilled in the art that the inventors had possession of the claimed invention at the time the application was filed.

Specifically, the Office Action alleges that claim 1 is drawn to a method employing two or more "structurally identical" and differentially isotopically labeled protein reagents while the specification teaches at page 10, lines 18-21 "substantially chemically identical" and differentially isotopically labeled protein reagents. Applicants have amended the claims to conform with the description in the specification. With regard to the use of the term "substantially chemically identical" in the amended claims, Applicants submit, as was discussed during the interview, that this phrase taken in context with the recitation of the first two lines of step (b) of claim 1 has meaning to those of skill in the relevant art. Further evidence can be found by the use of the same language in the Aebersold et al. reference cited in the Office Action. Applicants have amended claims 1 and 13 to further clarify the issues concerning the written description requirement.

Claims 1-22 were rejected under 35 U.S.C. §112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention.

*Appl. No. 09/851,058*

*Amendment dated July 1, 2004*

*Reply to Office Action of March 10, 2004*

Specifically, the Office Action alleges that the claims (particularly with reference to claim 1) are vague and indefinite because it is not clear how the set of two or more protein reagents recited in step 1(b) interact with the sample of step 1(a) and that such lack of clarity extends to the recitations in step 1(c). In addition, the Office Action asserts there is insufficient antecedent basis for the limitation "set of protein sample" recited in step 1(c). Applicants have amended claim 1 to further clarify the issues concerning vagueness and indefiniteness.

Applicants thus respectfully request reconsideration and withdrawal of the rejections of the amended claims under 35 U.S.C. §112, first and second paragraphs.

*Rejections Under 35 U.S.C. §103*

Claims 1-3, 6-9 and 10-21 were rejected under 35 U.S.C. §103 (a) as allegedly being obvious over Aebersold et al. (WO 00/11208) ("Aebersold") in view of Bienvenut et al. (Analytical Chemistry, 1999, 71, 4800-4807) ("Bienvenut").

Claim 1 has been amended to more clearly recite that the step of separating by electrophoresis protein reagents labeled as set forth in the presently amended claims occurs prior to digestion. Applicants respectfully submit that claim 1 and all claims dependent therefrom are novel and non-obvious because neither Aebersold nor Bienvenut, taken singly or in proper combination, teach this aspect of Applicants' invention.

Claims 4 and 5, which depend from claim 1, were also rejected under 35 U.S.C. 103(a) as allegedly being unpatentable over Aebersold in view of Bienvenut and in further view of Yates et al. (US Patent No. 5,538,897) ("Yates"), and claim 22 (also dependent on claim 1) was also rejected as being unpatentable over Aebersold in view of Bienvenut and in further view of Clauser et al. Applicants respectfully submit that neither Yates nor Clauser et al. provide the teaching missing in Aebersold and Bienvenut, and thus dependent claims 4, 5 and 22 are novel and non-obvious over the cited prior art.

Claims 1-8 and 10-21 were rejected under 35 U.S.C. §103(a) as allegedly being obvious over Aebersold in view of Gygi et al. The Office Action asserts that Gygi et al. discloses methods for quantitative protein analysis that combines protein separation by 2-D gel electrophoresis with mass spectrometry (see page 994, 1<sup>st</sup> column, 2<sup>nd</sup> paragraph and page 998 2<sup>nd</sup> column, last paragraph). The Gygi et al. reference, which is a paper based on the Aebersold et al. WO 00/11208 reference, however, does not teach or suggest providing a method for

*Appl. No. 09/851,058*

*Amendment dated July 1, 2004*

*Reply to Office Action of March 10, 2004*

quantitative protein analysis where substantially chemically identical and differentially isotopically labeled protein reagents are separated by electrophoresis prior to detection by mass spectrometry. Applicants thus respectfully submit that the presently amended claims are novel and non-obvious over Aebersold in view of Gygi et al. taken alone, or in proper combination.

Claim 9, which depends from claim 1, was also rejected under 35 U.S.C. §103(a) as allegedly being obvious over Aebersold in view of Gygi et al. and in further view of Bienvenut, dependent claim 22 (also dependent from claim 1) was also rejected under 35 U.S.C. §103(a) as allegedly being obvious over Aebersold in view of Gygi et al. and in further view of Clauser et al. For the reasons set forth above, Applicants respectfully submit that claims 9 and 22 are novel and non-obvious over the cited prior art.

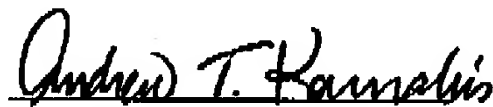
#### CONCLUSION

In view of above, it is believed that all presently pending claims are in condition for allowance, and it is respectfully requested that the application be passed to issue. If the Examiner feels that a telephone call would serve to clarify issues or expedite the prosecution of this case, the Examiner is invited to call the undersigned at (508) 383-7406.

Applicants believe no additional fee beyond the petition for extension of time is due with respect to this Amendment and Response. However, if any additional fee is due, please charge our Deposit Account No. 50-1191, under Case No. SYP-172, from which the undersigned is authorized to draw.

Dated: July 1, 2004

Respectfully submitted,



Andrew T. Karnakis, Esq.  
Attorney for Applicants, Reg. No. 27,909  
Applied Biosystems  
500 Old Connecticut Path  
Framingham, MA 01701  
Direct Phone: (508) 383-7406  
Facsimile: (508) 383-7468